This Week's Citation Classic®

Scandalios J G. Genetic control of multiple molecular forms of enzymes in plants: a review. *Biochem. Genet.* 3:37-79, 1969.
[MSU/AEC Plant Research Laboratory, Michigan State University, East Lansing, MI]

Using genetically variant enzymes as markers, it is possible to study allelic and nonallelic gene interactions during development and in populations in efforts to determine the evolutionary significance of enzyme multiplicity in metabolism. Once well-defined genetically and biochemically, such gene-enzyme systems could serve as useful models to investigate gene structure and function at a more molecular and mechanistic level. [The *SCI*® indicates that this paper has been cited in over 350 publications.]

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The premise of the research reported in this paper was that multiple molecular forms of enzymes (isozymes), if properly and rigorously studied, could serve as excellent and effective "built-in" biological markers to explore a variety of pertinent questions in genetics, biochemistry, physiology, and evolution. It pointed out that the accessibility and ease of utilizing the then-new techniques of gel electrophoresis and zymogram analyses could lead to rapid results, interpretations, and occasionally to some erroneous conclusions. The paper stressed the need, utilizing specific experimental data, to genetically and biochemically examine the nature of enzyme multiplicity in depth, employing not one, but all, available techniques before reaching conclusions. Experimental data were presented to indicate the utility of isozymes in studies of gene regulation and expression during development, tissue and temporal specificity of gene expression, enzyme structure and function, intracellular compartmentalization, evolution, and population biology. I attempted to synthesize from existing knowledge a path toward future research in the field.

The invitation to write this paper came from the editor of the journal *Biochemical Genetics* with the request that I summarize primarily results from my own laboratory as paradigms for the utility of isozymes in resolving basic biological questions. I had recently been invited to join the faculty of the new Atomic Energy Commission (now Department of Energy) Plant Research Laboratory at Michigan State University to continue my studies begun at the University of Hawaii in 1962. It was a very exciting time, and I was having fun at the bench. Nevertheless, I was convinced that this paper could be useful to colleagues entering the field and might encourage others to do so, as well as serve the needs of active investigators in the area. The first draft was written while I was a visiting professor of genetics at the University of California-Davis. Numerous colleagues who read it suggested that I include some of the basic experimental methods we had developed or refined for our studies, since other investigators would find them useful. Based on the numerous requests I was receiving on methodology, I too was convinced of this need; in consultation with the editor it was decided to include some of the methods as an appendix.

The frequency of citation of this paper is likely due to the simplicity and directness of the results presented and the fact that they have stood the test of time. To this date, I still receive requests for this paper. In addition, the appearance of this paper was timely. When I was invited to write it, I saw an opportunity to bring a number of developing trends into focus in a way that might be meaningful to the future development of the field. It is interesting to note that several of the systems discussed in this paper have been developed to the point where the genes have now been isolated and sequenced for purposes of further defining their structure and function by recombinant DNA techniques.[1,2]

It is difficult to pinpoint the exact reason for its accumulation of citations. Over the years, I have been told by colleagues that this paper helped to spark the development of plant biochemical and developmental genetics and fostered the effective use of isozymes in a great variety of plant biology studies. For my part, I feel privileged to have had the chance to participate in, and to glimpse the renaissance of, plant biology and molecular genetics. This paper was my integrative and interpretive recording of these early but continuing events. I am indeed happy to have authored a second *Citation Classic* (see reference 3 for my first) and hope it will continue to serve a useful purpose.

1. **Scandalios J G.** The antioxidant enzyme genes *Cat* and *Sod* of maize: regulation, functional significance, and molecular biology. *Isozymes—Curr. Top. Biol. Med. R.* 14:19-44, 1987.
2. **Cannon R E, White J A & Scandalios J G.** Cloning of cDNA for maize superoxide dismutase-2 (SOD-2). *Proc. Nat. Acad. Sci. USA* 84:179-83, 1987.
3. **Scandalios J G.** Citation Classic. Commentary on *Annu. Rev. Plant Physiol.* 25:255-8, 1974. (Cited 185 times.) (Barrett J T, ed.) *Contemporary classics in plant, animal, and environmental sciences.* Philadelphia: ISI Press, 1986. p. 319.

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